ORIGINAL ARTICLE

Is local resection adequate for T1 stage ampullary cancer?

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Abstract

Background: Concerns for morbidity after a pancreaticoduodenectomy (PD) has led to practitioners adopting endoscopic resection or ampullectomy in the treatment of T1 ampullary cancer (AC). It was hypothesized that survival for patients undergoing local resection of AC was inferior to those undergoing a PD.

Methods: All the data of patients with AC reported in the Surveillance, Epidemiology and End Results (SEER) database between 2004 and 2010 were collected. Five-year survival rates according to nodal disease and histological type were compared.

Results: There were 1916 cases of AC; 421 (22%) had T1 disease. Among those with T1 disease, 217 (51%) received endoscopic surveillance, 21 (5%) underwent local resection/ampullectomy, 20 (5%) underwent ampullectomy with regional lymphadenectomy and 163 (39%) underwent PD. For patients with complete nodal staging (PD, n = 163), 35 (22%) had metastatic disease in the nodes. Grade was significantly associated with node positivity ($P = 0.007$). In multivariate models, survival was improved with either an ampullectomy with regional lymphadenectomy [hazard ratio (HR) 0.19; 95% confidence interval (CI) 0.05–0.61, $P < 0.005$] or a PD (HR 0.23; 95% CI 0.15–0.36, $P < 0.001$).

Conclusion: Patients with T1 AC have a high risk for nodal metastases especially if they are higher-grade lesions. Nodal clearance with a lymphadenectomy or a PD is essential for long-term survival in these patients.

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Introduction

Adenocarcinoma of the ampulla of Vater (AC) is a relatively uncommon malignancy with an incidence of less than 1% of all gastrointestinal malignancies. It is the second most common cancer arising in the periampullary region comprising 6–20% of periampullary tumours.[1–3] Unlike pancreatic adenocarcinoma, AC has a more favourable prognosis with 5-year survival rates ranging from 30–60% after surgery.[4–6] The improved outcomes of AC compared with pancreatic adenocarcinoma have been largely attributed to the higher rate of tumour resectability, more favourable histology, as well as less likelihood for lymphatic and perineural invasion.[7] Currently, resection remains the only curative therapy option for AC.

Cancers of the ampulla are usually reported as single institutional experiences with relatively small sample sizes, and only a few have examined survival beyond 5 years.[3–8] This approach often makes it difficult to exclude institutional variability in diagnostic criteria, clinical outcome and selection bias. The development of national health registries has provided a more rapid means of access to the accumulation of population-based histopathological and clinical data. Such data have been catalogued according to site, morphological and clinical nomenclatures. Initiated in 1973, the Surveillance, Epidemiology and End Results Registry (SEER) of the National Cancer Institute is one such registry, now robust enough, where clinical and descriptive characteristics of uncommon tumours can be assessed at a population level.[9,10]

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AC is widely treated by a pancreaticoduodenectomy (PD) because of its propensity to spread to lymph nodes and a high incidence of recurrence.[11] Fit patients with tumours exhibiting high-grade dysplasia or adenocarcinoma are generally treated by PD with low recurrence rates.[12] Recent series report 5-year post-operative survival rates of 53–68%.[13] The peri-operative mortality rate for PD has declined and is widely accepted at high volume centres where the procedure is routinely performed, but morbidity after PD remains high.[14] Local resection is a less invasive and potentially equally effective alternative for cancers with favourable prognostic features.[15] Local resection of ampullary tumours has been performed for a century but remains controversial. The use of this procedure for benign conditions is clear, but its place, if any, in the management of AC remains ill defined. Successful endoscopic removal of T1 cancers has also been reported but is not widely practiced.[16–18] Selection criteria have been suggested and small series in high-risk individuals have been reported. The aim of this study was to investigate the outcomes of endoscopic and local resection of AC by comparison with PD. We hypothesized that survival for patients undergoing endoscopic or local resection of AC was inferior to those undergoing a PD.

Patients and methods

A retrospective cohort study was performed utilizing the SEER database. Patients with pathologically confirmed AC from 2004 to 2010 were identified by ICD-3 histology codes 8140/3, adenocarcinoma not otherwise specified (NOS), combined with site code C24.1, ampulla of Vater. Inclusion criteria required that patients have T1 disease by American Joint Committee on Cancer (AJCC) staging (tumour limited to the ampulla of Vater or sphincter of oddi) and no evidence of metastatic disease. Inclusion was restricted to 2004 onwards, owing to the improvements in the staging variables and the inclusion of the CS Extension variables. Patients with incomplete AJCC staging and neoplasms other than adenocarcinoma were excluded from the analysis. Data were abstracted using the SEER*Stat software, version 8.0.4, National Cancer Institute, Washington, DC, USA.

Clinicopathological characteristics obtained included TNM stage, histological type, patient demographics, adjuvant radiation and type of resection. The patient cohort was stratified by extent of resection. Extent of surgery was classified into four groups: (i) endoscopic surveillance/ no surgery, (ii) local resection/ ampullectomy without a lymphadenectomy, (iii) ampullectomy with a lymphadenectomy, and (4) radical resection (PD). Endoscopic surveillance/no resection was defined according to the SEER 2013 surgery coding manual as no surgery of the primary site (code 00 or code 10–14 which include destruction of tumor with ablation/photodynamic therapy/cryotherapy with no pathology specimen). A local resection was defined as partial to total surgical removal of the primary tumour (codes 20–30). A radical resection (PD) was defined as total removal of the primary site with resection of adjacent organs (code 40 to 60). Local resection was also subclassified according to performance of a lymphadenectomy. The SEER database codes lymph nodes based on assessment at final pathology. They are coded by the number of lymph nodes and not location of the lymph node.

Statistical analysis

Statistical analyses were performed with Stata/MP 10.0 for Windows (StataCorp, College Station, TX, USA). Alpha was set at 0.05. The Kruskal–Wallis test was used for non-parametric analysis of continuous variables, whereas categorical variables were analysed with the chi-squared test. Survival was assessed with the Kaplan–Meier method, and Cox proportional hazards models were used to assess independent predictors of survival. The overall survival time (OS) was calculated from the time of surgery to the time of death as defined by the SEER registry.

Results

Patient characteristics

From 2004–2010, there were 1916 cases of ampullary cancer; 421 (22%) had T1 disease. The median age at diagnosis was 77 years [interquartile range (IQR): 67.5–83]. The majority of patients were male (n = 225, 52%) and white (n = 356, 82%). The demographic, clinical and tumour-specific pathological characteristics between treatment groups are presented in Table 1.

Tumour characteristics

The median tumour size for the entire cohort was 1.5 cm (1.0–2.2), which was significantly larger in the surveillance only arm ($P < 0.001$, Table 1). The median number of nodes examined in patients undergoing a radical resection (PD) was 10 (4–16). For patients with complete nodal staging (PD, n = 163), 35 (22%) had metastatic disease in the nodes. Histological grade was missing in 21% (n = 91) of the collective cohort. Grade was significantly associated with node positivity with 10% positivity in well-differentiated (n = 61), 12% in moderately-differentiated (n = 163), and 27% in poorly-differentiated tumours (n = 85; P = 0.007). Tumour size ≥1 cm was not associated with node positivity (P = 0.95).

Therapy characteristics

Of the 421 patients, 217 (51%) received surveillance/endoscopic treatment only, 21 (5%) underwent local resection/ampullectomy alone, 20 (5%) underwent ampullectomy with regional lymphadenectomy and 163 (39%) underwent a PD. The majority of the patients in the surveillance arm were not recommended for surgery (n = 155, 71%), whereas 29 (13%) patients refused surgery. No patients received fulguration/cryotherapy/ photodynamic therapy. Radiation was administered more frequently in patients with node positive disease (27% versus 11%, P = 0.001) and in those undergoing a lymphadenectomy (Table 1).

Effect of prognostic factors on survival

Patients undergoing radical surgery had a significantly improved overall survival (mean survival 5 versus 2 years for those with

Table 1 Demographics and clinical and tumour-specific pathological characteristics between treatment groups

Variable	Endoscopic Surveillance/ No Surgery (n = 217)	Local Resection (No Lymphadenectomy) (n = 21)	Local Resection with lymphadenectomy (n = 20)	Radical Resection (n = 163)	P-value
Age (years)	81 (75–85)	84 (72–89)	64 (57–73)	72 (62–77)	0.0001[a]
Male gender	114 (52%)	9 (43%)	11 (55%)	85 (52%)	0.85
Grade (n = 321)					
Well differentiated	24 (18%)	5 (29%)	6 (33%)	32 (21%)	0.79
Moderately differentiated	68 (51%)	8 (47%)	9 (50%)	80 (53%)	
Poorly differentiated	41 (31%)	4 (24%)	3 (17%)	40 (26%)	
Undifferentiated	1 (0.7%)	0 (0%)	0 (0%)	0 (0%)	
Race					
White	185 (85%)	14 (67%)	17 (85%)	130 (80%)	0.01[a]
Black	16 (7%)	1 (5%)	2 (10%)	6 (4%)	
Other	16 (7%)	6 (28%)	1 (5%)	27 (16%)	
Radiation					
No radiation	216 (99%)	19 (90%)	14 (70%)	141 (86%)	<0.001[a]
Adjuvant radiation	1 (0.4%)	2 (9%)	5 (25%)	22 (13%)	
Neoadjuvant radiation	–	0 (0%)	1 (5%)	0 (0%)	
Median number of lymph nodes examined	–	–	12 (5–17)	10 (4–16)	0.38
1 lymph node positive	–	–	0	16 (10%)	
≥2 lymph nodes positive	–	–	4 (20%)	19 (12%)	
Tumour size (cm)	2 (1.5–3)	2 (1.1–3)	1.5 (1–2)	1.3 (9-2)	0.001[a]
Median survival (months)	16 (12–22)	58 (16-)	Not reached	Not reached	
Mean survival (restricted to longest follow-up time in months) [mean(SE)]	24 (2.5)	55 (9.2)	53 (6.4)	64 (2.7)	
Mean survival in months (exponentially declined to zero, mean)	31 (= 2.5 years)	87 (= 7.2 years)	199 (= 16.5 years)	229 (= 18 years)	

[a]Statistically significant at alpha = 0.05.

surveillance alone, $P < 0.001$, Table 1). The median survival was not reached for those undergoing a lymphadenectomy, and hence we modelled mean survival assuming either censorship at last month of follow-up or exponentially assuming the rate of death to be constant (Table 1). Unadjusted Kaplan–Meier curves showed improved survival with all resection arms compared with surveillance/ no resection (Fig. 1). However, after adjusting for demographic characteristics, node positivity was significantly associated with a worse survival [hazard ratio (HR) 2.2; 95% confidence interval(CI) 1.3–3.8, $P = 0.003$] in multivariate models. We chose not to include node positivity in our models trying to assess the effect of surgical resection, as node status was not assessed for surveillance/ endoscopic resection or local resection only arms. Survival was improved with either an ampullectomy with regional lymphadenectomy (HR 0.19; 95% CI 0.05–0.61, $P < 0.005$) or a PD (HR 0.23; 95% CI 0.15–0.36, $P < 0.001$) in multivariate models adjusted for age, gender, race, radiation therapy and tumour size (Table 2). Although local resection without lymphadenectomy did show improved survival, the change in hazard ratio as compared with surveillance/no resection was not as great as the regional lymphadenectomy or PD groups (HR 0.33; 95% CI 0.13–0.82, $P < 0.02$).

Discussion

In recent years, the increasing experience with endoscopy and otherwise low morbidity rates associated with this technique for the management of ampullary masses has resulted in some studies suggesting that T1 ACs may be approached by less invasive means.[17–19] Some surgeons have also proposed performing limited resections for early stage AC in order to circumvent the potential morbidity associated with a radical resection.[20,21] However, the relative scarcity of the disease has created difficulties when attempting to assess outcomes after the surgical management of AC. Most studies suffer from small sample sizes or provide aggregate data on 'peri-ampullary' neoplasms.[17,22–24] Evidence of

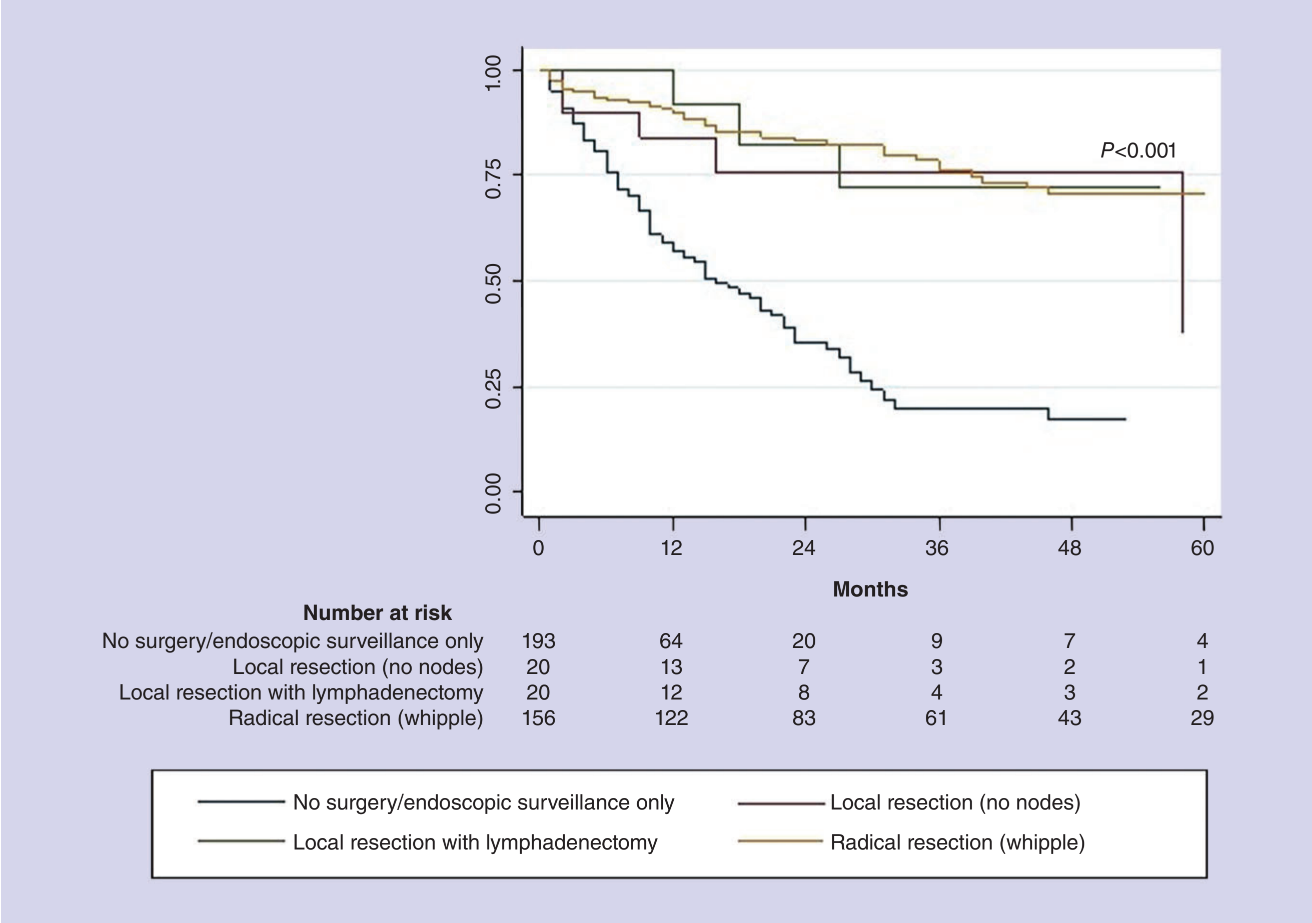

Figure 1 Overall survival by surgery type for T1 ampullary adenocarcinoma

oncological equivalence for endoscopic or local resection when compared with a radical resection is also lacking. Therefore we sought to utilize the SEER Registry to capture a larger cohort of patients in attempt to better understand the disease, and critically assess the management of patients with early stage AC. In the present study, patients with T1 disease demonstrated a high level of lymph node metastases thereby highlighting the importance of a lymphadenectomy in this patient cohort. More importantly, data from this study provides important information on the survival of patients after resection of AC. Specifically, the present study reveals that endoscopic surveillance and ampullectomy without a lymphadenectomy can result in suboptimal outcomes.

Currently there is insufficient data to determine if an extended resection aids only in staging or if it contributes to increased cure rates. Among patients with AC, one of the most important clinicopathological variables to influence survival is the presence of lymph node metastasis.[22,25] In fact, the presence of lymph node metastasis was associated with a median survival of 36 months compared with a median survival not reached at current follow-up. An adequate lymph node dissection at the time of surgery for AC not only provides important prognostic information, but also may decrease the risk of local recurrence.[26] Park *et al.* showed that lymph node metastasis was the most important risk factor for recurrence after a curative resection.[27] Branum *et al.* reported that six out of eight patients developed a recurrence after a local ampullectomy.[28] Lindell *et al.* showed that local recurrence was diagnosed in 22% of patients after PD as compared with 80% of patients after local resection (P = 0.001).[29] Feng *et al.* reported tumour recurrence in 23.3% of patients after a PD and 48.0% of patients after local resection (P = 0.035).[30] Although in the present study recurrence data were unable to be captured, the significant improvement in overall survival for the cohort of patients that underwent a lymphadenectomy suggests that adequate tumour extirpation is also contingent upon clearing of the local lymph nodes.

Certainly staging is also important in directing patients towards appropriate adjuvant therapies. Some authors have suggested that an ampullectomy without a lymphadenectomy is an adequate therapy for patients with T1 AC owing to the low incidence of lymph node metastasis.[31–33] However, data from this study found

Table 2 Uni- and multivariate analysis of overall survival for patients with ampullary adenocarcinoma

Variable	Univariate Hazards (95% CI)	*P*-value	Multivariate Hazards (95% CI)	*P*-value
Age at diagnosis	1.03 (1.01–1.05)	<0.001[a]	1.01 (0.99–1.02)	0.19
Female gender	1.12 (0.80–1.57)	0.49	1.05 (0.74–1.49)	0.78
White	–		1	
Black	0.96 (0.48–1.89)	0.91	1.0 (0.50–1.99)	1.0
Other	0.64 (0.36–1.13)	0.13	0.69 (0.38–1.22)	0.20
Grade (n = 321)			Excluded due to missing data	
Well differentiated	1		–	
Moderately differentiated	0.98 (0.59–1.63)	0.96	–	
Poorly Differentiated	1.24 (0.72–2.17)	0.43	–	
Tumour size (*n* = 243)			Excluded due to missing data	
Tumour size <1 cm	1		–	
Tumour size ≥1 cm	1.52 (0.77–2.99)	0.23	–	
Resection type				
Surveillance only	1	1	1	
Local resection (no lymph nodes)	0.31 ((0.12–0.76)	0.01[a]	0.33 (0.13–0.82)	0.02[a]
Local resection with lymphadenectomy	0.18 (0.05–0.56)	0.003[a]	0.19 (0.05–0.61)	0.005[a]
Radical resection	0.19 (0.13–0.30)	<0.001[a]	0.23 (0.15–0.36)	<0.001[a]
No radiation	–		1	
Radiation	1.37 (0.89–2.09)	0.14	1.2 (0.76–1.80)	0.462

[a]Statistically significant at alpha = 0.05.

this decidedly not to be the case. Although the risk of lymph node metastasis increased with worse histology, the incidence of lymph node metastasis was still clinically significant in patients with T1 disease (10%–27.0%). Our findings are consistent with data from smaller series that have noted an incidence of lymph node metastasis of 20% to 25% for patients with T1–T2 disease.[22] Lindell *et al.* analysed 92 patients with cancer of the ampulla of Vater and demonstrated a 5-year survival of 10% for patients undergoing only local resection. The authors concluded that local resection played a limited role in carefully selected patients.[29] These data strongly suggest that even patients with early AC have a high risk of lymph node metastasis and are best served with an operation that includes lymph node dissection and clearance. Although our study showed similar survival with PD or local ampullectomy with a lymphadenectomy, our institutional bias is to favour PD rather than local ampullectomy with a lymphadenectomy in appropriate surgical candidates because the mortality associated with a PD is low when performed at high-volume centres.[34]

The present study has several limitations inherent to any population-based registry. Although the SEER database allows for longitudinal examination of population-based cancer data, it lacks comprehensive outpatient data such as the use of adjuvant chemotherapy, presence of pre-existing comorbidities and tumour margin status. Other parameters including perineural and lymphovascular invasion that have been identified by others as important predictors of outcome are not included for evaluation in SEER. In addition, the surgical operative and endoscopic procedure notes are not available for review. Therefore, the location of lymph nodes examined in the ampullectomy with the lymphadenectomy group is unknown. The ampullectomy groups also have small sample sizes which may have influenced their overall survival. Additionally, whether or not endoscopic resections were truly for curative intent versus diagnostic alone may explain the worse survivals in the endoscopic surveillance group. It may also be as a result of selection bias as the 71% that were not offered surgical resection may not have been appropriate surgical candidates owing to the presence of comorbidities and older age. Lastly, this study is limited by the inability to capture recurrence data. However, the strengths of SEER remains in its ability to broadly cross-section the true population, capture a large cohort of patients with rare diseases and assess current trends in the medical community.

In conclusion, the present study is a national, population-based analysis of outcomes for AC. Our research confirms a high level of lymph node metastases and highlights the importance of a lymphadenectomy in those patients with T1 ACs. More importantly, our data shows that endoscopic surveillance and ampullectomy without a lymphadenectomy can result in suboptimal outcomes. Although our study showed a similar survival with PD or local ampullectomy with a lymphadenectomy, our institutional bias is to favour PD rather than local ampullectomy with a lymphadenectomy in appropriate surgical candidates because the mortality associated with a PD is low when performed at high-volume centres.

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Conflicts of interest

None declared.

References

1. Bouvet M, Gamagami RA, Gilpin EA, Romeo O, Sasson A, Easter DW *et al*. (2000) Factors influencing survival after resection for periampullary neoplasms. *Am J Surg* 180:13–17.
2. Chareton B, Coiffic J, Landen S, Bardaxoglou E, Campion JP, Launois B. (1996) Diagnosis and therapy for ampullary tumors: 63 cases. *World J Surg* 20:707–712.
3. Talamini MA, Moesinger RC, Pitt HA, Sohn TA, Hruban RH, Lillemoe KD *et al*. (1997) Adenocarcinoma of the ampulla of vater. A 28-year experience. *Ann Surg* 225:590–600.
4. Sarmiento JM, Nagomey DM, Sarr MG, Farnell MB. (2001) Periampullary cancers: are there differences? *Surg Clin North Am* 81:543–555.
5. Duffy JP, Hines OJ, Liu JH, Ko CY, Cortina G, Isacoff WH *et al*. (2003) Improved survival for adenocarcinoma of the ampulla of Vater: fifty-five consecutive resections. *Arch Surg* 138:941–948; discussion 948–950.
6. Allema JH, Reinders ME, van Gulik TM, van Leeuwen DJ, Verbeek PC, de Wit LT *et al*. (1995) Results of pancreaticoduodenectomy for ampullary carcinoma and analysis of prognostic factors for survival. *Surgery* 117:247–253.
7. Klempnauer J, Ridder GJ, Pichlmayr R. (1995) Prognostic factors after resection of ampullary carcinoma: multivariate survival analysis in comparison with ductal cancer of the pancreatic head. *Br J Surg* 82:1686–1691.
8. Howe JR, Klimstra DS, Moccia RD, Conlon KC, Brennan MF. (1998) Factors predictive of survival in ampullary carcinoma. *Ann Surg* 228:87–94.
9. Surveillance, Epidemiology, and End Results (SEER) Program. Public-Use Data (2004–2010), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, based on the November 2012 submission. Available at http://www.seer.cancer.gov/.
10. Albores-Saavedra J, Schwartz AM, Batich K, Henson DE. (2009) Cancers of the ampulla of vater: demographics, morphology, and survival based on 5,625 cases from the SEER program. *J Surg Oncol* 100:598–605.
11. Brown KM, Tompkins AJ, Yong S, Aranha GV, Shoup M. (2005) Pancreaticoduodenectomy is curative in the majority of patients with node-negative ampullary cancer. *Arch Surg* 140:529–532.
12. Tran TC, Vitale GC. (2004) Ampullary tumors: endoscopic versus operative management. *Surg Innov* 11:255–263.
13. Schmidt CM, Powell ES, Yiannoutsos CT, Howard TJ, Wiebke EA, Wiesenauer CA *et al*. (2004) Pancreaticoduodenectomy: a 20-year experience in 516 patients. *Arch Surg* 139:718–725.
14. Strasberg SM, Drebin JA, Mokadam NA, Green DW, Jones KL, Ehlers JP *et al*. (2002) Prospective trial of a blood supplybased technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure. *J Am Coll Surg* 194:746–758.
15. Park JS, Yoon DS, Park YN, Lee WJ, Chi HS, Kim BR. (2007) Transduodenal local resection for low-risk group ampulla of vater carcinoma. *J Laparoendosc Adv Surg Tech A* 17:737–742.
16. Yoon SM, Kim MH, Kim MJ, Jang SJ, Lee TY, Kwon S *et al*. (2007) Focal early stage cancer in ampullary adenoma: surgery or endoscopic papillectomy? *Gastrointest Endosc* 66:701–707.
17. Yoon YS, Kim SW, Park SJ, Lee HS, Jang JY, Choi MG *et al*. (2005) Clinicopathologic analysis of early ampullary cancers with a focus on the feasibility of ampullectomy. *Ann Surg* 242:92–100.
18. Woo SM, Ryu JK, Lee SH, Lee WJ, Hwang JH, Yoo JW *et al*. (2009) Feasibility of endoscopic papillectomy in early stage ampulla of Vater cancer. *J Gastroenterol Hepatol* 24:120–124.
19. Jung MK, Cho CM, Park SY, Jeon SW, Tak WY, Kweon YO *et al*. (2009) Endoscopic resection of ampullary neoplasms: a single-center experience. *Surg Endosc* 23:2568–2574.
20. Beger HG, Treitschke F, Gansauge F, Harada N, Hiki N, Mattfeldt T. (1999) Tumor of the ampulla of Vater: experience with local or radical resection in 171 consecutively treated patients. *Arch Surg* 134:526–532.
21. Rattner DW, Fernandez-del Castillo C, Brugge WR, Warshaw AL. (1996) Defining the criteria for local resection of ampullary neoplasms. *Arch Surg* 131:366–371.
22. Barauskas G, Gulbinas A, Pranys D, Dambrauskas Z, Pundzius J. (2008) Tumor-related factors and patient's age influence survival after resection for ampullary adenocarcinoma. *J Hepatobiliary Pancreat Surg* 15:423–428.
23. Fathy O, Abdel-Wahab M, Elghwalby N, Sultan A, El-Ebidy G, Abu-Zeid M *et al*. (2008) Surgical management of peri-ampullary tumors: a retrospective study. *Hepatogastroenterology* 55:1463–1469.
24. Yeo CJ, Cameron JL, Sohn TA, Lillemoe KD, Pitt HA, Talamini MA *et al*. (1997) Six hundred fifty consecutive pancreaticoduodenectomies in the 1990s: pathology, complications, and outcomes. *Ann Surg* 226:248–257.
25. Qiao QL, Zhao YG, Ye ML, Yang YM, Zhao JX, Huang YT *et al*. (2007) Carcinoma of the ampulla of Vater: factors influencing long-term survival of 127 patients with resection. *World J Surg* 31:137–143.
26. Bottger TC, Boddin J, Heintz A, Junginger T. (1997) Clinicopathologic study for the assessment of resection for ampullary carcinoma. *World J Surg* 21:379–383.
27. Park JS, Yoon DS, Kim KS, Choi JS, Lee WJ, Chi HS *et al*. (2007) Factors influencing recurrence after curative resection for ampulla of Vater carcinoma. *J Surg Oncol* 95:286–290.
28. Branum GD, Pappas TN, Meyers WC. (1996) The management of tumors of the ampulla of Vater by local resection. *Ann Surg* 224:621–627.
29. Lindell G, Borch K, Tingstedt B, Enell EL, Ihse I. (2003) Management of cancer of the ampulla of Vater: does local resection play a role? *Dig Surg* 20:511–515.
30. Feng JF, Zhou XM, Mao WM. (2012) Prognostic analysis of carcinoma of the ampulla of Vater: pancreaticoduodenectomy versus local resection. *Hippokratia* 16:23–28.
31. Demetriades H, Zacharakis E, Kirou I, Pramateftakis MG, Sapidis N, Kanellos I *et al*. (2006) Local excision as a treatment for tumors of ampulla of Vater. *World J Surg Oncol* 4:14.
32. Nikfarjam M, Muralidharan V, McLean C, Christophi C. (2001) Local resection of ampullary adenocarcinomas of the duodenum. *ANZ J Surg* 71:529–533.
33. Dixon E, Vollmer CM Jr, Sahajpal A, Cattral MS, Grant DR, Taylor BR *et al*. (2005) Transduodenal resection of peri-ampullary lesions. *World J Surg* 29:649–652.
34. Sosa JA, Bowman HM, Gordon TA, Bass EB, Yeo CJ, Lillemoe KD *et al*. (1998) Importance of hospital volume in the overall management of pancreatic cancer. *Ann Surg* 228:429–438.